

Methods. Subjects with moderate to severe MDD at baseline per their HAM-D17 or PHQ-9 scores were included in the analysis for the RCT (n=261) and real-world data (n=242). In both studies, 8-week response and remission rates were analyzed for patients using IDgenetix-guided medication management (Guided) compared to patients receiving standard of care (Unguided).

Results. Patient response and remission rates strongly aligned between both studies. Response rates for the IDgenetix-guided participants in the RCT were 49% compared to 58% in the real-world data. Remission rates in the Guided group were 31% in both the RCT and real-world study compared to 22% and 19%, respectively, for participants in the Unguided group.

Conclusions. Comparing the clinical outcome results from the RCT with real-world data demonstrated the consistent impact of IDgenetix on patient response and remission rates. This study provides robust evidence-based research that supports the clinical use of IDgenetix to guide medication management in patients with MDD.

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Centanafadine Sustained Release Is Efficacious in Patients with Adult ADHD, Regardless of Their Treatment History

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Introduction. Centanafadine (CTN) is a potential first-in-class norepinephrine/dopamine/serotonin triple reuptake inhibitor (NDSRI) that has demonstrated efficacy, safety, and tolerability vs placebo (PBO) in adults with ADHD in 2 pivotal phase 3 trials (Adler LA, et al. J Clin Psychopharmacol. 2022;42:429-39).

Methods. Pooled data from 2 double-blind, multicenter, PBO-controlled trials enrolling adults (18–55 years) meeting DSM-5 ADHD criteria were analyzed. Patients were randomized 1:1:1 to CTN sustained release (SR) 200 mg or 400 mg total daily dose (TDD) or matching PBO if Adult ADHD Investigator Symptom Rating Scale (AISRS) score was ≥ 28 at screening (if not receiving pharmacologic ADHD treatment) or ≥ 22 at screening and ≥ 28 at baseline (if receiving treatment). Having had no prior benefit from ≥ 2 ADHD therapies of different classes, use of prohibited medications, and positive alcohol/drug screens were exclusionary. Studies had 4 periods: (1) screening and washout (≤ 28 days), (2) single-blind PBO run-in (1 week), (3) double-blind treatment (6 weeks), and (4) follow-up (10 days after last dose). Patients with $\geq 30\%$ Adult ADHD Self-report Scale (ASRS) improvement from start to end of screening were screen failures; those with $\geq 30\%$ ASRS improvement from start to end of PBO run-in were terminated early. A mixed model for repeated measures analysis evaluated CTN SR vs PBO based on ADHD treatment history; least

squares mean (LSM) change from baseline (BL) in AISRS at day 42 was the outcome of interest.

Results. In total, 859 patients were analyzed (CTN SR 200 mg TDD, n=287; 400 mg TDD, n=287; PBO, n=285). LSM change from BL in AISRS score was significant at day 42 for each CTN SR TDD group (both, $P < 0.001$) in the overall population vs PBO. Among patients with prior stimulant/nonstimulant treatment (n=542), LSM change from BL was significant at day 42 vs PBO in the CTN SR 200 mg ($P=0.016$) and 400 mg ($P=0.008$) TDD groups. Although cohort size was limited (n=47), LSM change from baseline with CTN SR 400 mg TDD was significant ($P < 0.05$) from days 14 to 42 in those who took 2 prior stimulant/nonstimulant treatments, with $P=0.030$ at day 42. In those with no prior stimulant/nonstimulant treatment (n=317), LSM change from BL was significant at day 42 for the CTN SR 200 mg ($P=0.007$) and 400 mg ($P=0.008$) TDD groups vs PBO. When analyzed by history of any past stimulant use, LSM change from BL was significant at day 42 for CTN 200 mg (n=179; $P=0.013$) and 400 mg (n=166; $P=0.006$), with significance ($P < 0.05$) noted at day 7 (200 mg TDD) and at day 21 (400 mg TDD), remaining significant to day 42.

Conclusions. This pooled analysis suggests that CTN SR treatment is efficacious in adults with ADHD, regardless of prior treatments, an encouraging finding given reported adult ADHD treatment patterns.

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The Use of Carbamazepine in the Management of Psychogenic Nonepileptic Seizures (PNES)

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Psychogenic nonepileptic seizures (PNES) is a conversion disorder subtype that cause motor, sensory, autonomic, and cognitive symptoms that superficially resemble ictal epileptiform activity but without the electroencephalographic (EEG) activity that defines epilepsy. While 10-20% of patients referred to epilepsy centers are estimated to have PNES (1), diagnosing the condition is labor intensive as it requires seizure-like behavior observed during EEG monitoring. However, accurate diagnosis is essential as psychopharmacologic interventions have been shown to have limited utility in reducing seizure-like activity in PNES (2). Instead, case reports and small randomized clinical control trials have shown cognitive behavioral therapy (CBT) effective (3), and it is considered main stay of treatment.

We present the case of a 37-year-old woman who presented to our clinic with symptoms of depression including hypersomnia and anhedonia. Her most distressing symptoms were episodes of abnormal movements and shaking without loss of consciousness. She has a past medical history notable for EEG-confirmed PNES, major depressive disorder with psychotic features, generalized

anxiety disorder, clipped-intracranial aneurysm. She had been taking Duloxetine for major depressive disorder and fibromyalgia, and Carbamazepine was initiated to manage abnormal movements and her depressive symptoms. She reported improvement in the frequency and severity of abnormal movements after initiating Carbamazepine. Unfortunately, her depression worsened, and she was admitted to the inpatient unit for suicidal ideation and auditory and visual hallucinations commanding her to end her life. She was initiated on Aripiprazole. She was admitted for four days and was discharged after she demonstrated improvement in mood and severity of auditory hallucinations.

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Solriamfetol for Excessive Sleepiness in Narcolepsy and Obstructive Sleep Apnea: Effect Sizes and Numbers Needed to Treat or Harm

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Introduction. Solriamfetol (Sunosi[®]), a dopamine/norepinephrine reuptake inhibitor that has been shown to activate TAAR1, is approved (US and EU) to treat excessive daytime sleepiness (EDS) in adults with narcolepsy (75-150 mg/day) or obstructive sleep apnea (OSA) (37.5-150 mg/day). Effect size, number needed to treat (NNT) and number needed to harm (NNH) are statistical representations of efficacy and tolerability that clinicians may find helpful in guiding treatment decisions. This analysis characterized these statistical parameters from two registrational studies.

Methods. Post-hoc analysis of data from two phase 3 studies in adults with excessive daytime sleepiness associated with narcolepsy (TONES 2) or obstructive sleep apnea (TONES 3). Effect size compared to placebo, NNT, and NNH were calculated based on previously published endpoints, post-hoc analyses, and adverse events.

Results. On the maintenance of wakefulness test (MWT), effect size compared to placebo (*Cohen's d*) was 0.29, 0.82, and 1.13 for 75mg, 150mg, and 300mg doses of solriamfetol in TONES 2 and 0.46, 0.89, 1.08, and 1.28 for 37.5mg, 75mg, 150mg, and 300mg, respectively. On the Epworth sleepiness scale (ESS), *d* was 0.47,

0.80, and 1.02 for 75mg, 150mg, and 300mg doses in TONES 2, and 0.42, 0.37, 0.99, and 1.04 for 37.5mg, 75mg, 150mg, and 300mg doses in TONES 3. NNT for patients achieving an ESS ≤ 10 was 7, 5, and 3 for 75mg, 150mg, and 300mg doses in TONES 2 and 8, 6, 4, and 3 for 37.5mg, 75mg, 150mg, and 300mg doses in TONES 3. On the patient global impression of change (PGIC), NNT was 4, 3, and 3 for 75mg, 150mg, and 300mg doses in TONES 2 and 16, 5, 3, and 3 for 37.5, 75mg, 150mg, and 300mg in TONES 3. Similar NNT were found for the clinician global impression of change (CGIC) as for the PGIC. In both TONES 2 and TONES 3, NNH pooled across doses for adverse events occurring in at least 5% of patients and greater than placebo were all >10 , with the exception for headache in TONES 2 (NNH=6).

Conclusion. This post-hoc analysis demonstrates favorable effect size, NNT and NNH values for solriamfetol in the treatment of EDS associated with narcolepsy and OSA.

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Comparison of the Literature Regarding Weight Gain Between Olanzapine/Metformin and Olanzapine/Samidorphan Combinations

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Introduction. Many potent antipsychotics, such as olanzapine (OLZ), can cause significant and rapid weight gain as a potential side effect. This can lead to medication non-adherence and recurrence of psychiatric outcomes, or developing cardiometabolic risk factors that increase the risk of heart disease. The olanzapine-samidorphan (OLZ/SAM) drug combination has demonstrated ability to mitigate the weight gain caused by OLZ. However, olanzapine-metformin (OLZ/MET) combinations have also been studied for weight gain problems before the introduction of OLZ/SAM. The authors will review the similarities and differences between OLZ/SAM and OLZ/MET combinations regarding weight gain.

Methods. In this literature review, we conducted a non-systematic search in PubMed and Google Scholar, utilizing specific key words, such as "Olanzapine", "Metformin", "Samidorphan", and "Weight Gain." Case reports/series and narrative reviews were excluded, and only English-language studies reporting weight change or rate of weight change outcomes were included. Data extraction and qualitative synthesis were performed for the selected studies.

Results. OLZ/SAM has shown the ability to effectively reduce weight gain in non-obese populations, however, OLZ/MET has shown the ability to decrease weight gain in both obese and non-